PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing *(day/month/year)*	27 JUNE 2005 (27.06.2005)
Applicant's or agent's file reference 5FPO-03-18	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/KR2005/000969	01 APRIL 2005 (01.04.2005)	01 APRIL 2004 (01.04.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC7 C12N 15/63

Applicant

EWHA UNIVERSITY-INDUSTRY COLLABORATION FOUNDATION et al

1. This opinion contains indications relating to the following items:

- [x] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [x] Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.
For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/KR	Date of completion of this opinion	Authorized officer
Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	27 JUNE 2005 (27.06.2005)	AHN, Kyu Jeong Telephone No.82-42-481-5020

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material
   - ☒ a sequence listing
   - ☐ table(s) related to the sequence listing

   b. format of material
   - ☐ on paper
   - ☒ in electronic form

   c. time of filing/furnishing
   - ☒ contained in the international application as filed.
   - ☒ filed together with the international application in electronic form.
   - ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additioanl copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-13	YES
	Claims	None	NO
Inventive step (IS)	Claims	None	YES
	Claims	1-13	NO
Industrial applicability (IA)	Claims	1-13	YES
	Claims	None	NO

2. Citations and explanations :

The following documents have been considered for the purpose of this written opinion:

D1: Behav. Brain Res., Vol.136(2):503-509
D2: J. Biol. Chem., Vol.270(47):28257-28267
D3: Neurobiol. Dis., Vol.12(2):110-120
D4: Neurobiol. Aging, Vol.17(2):215-222

1. Novelty and Inventive Step

The present invention relates to a transgenic animal having Alzheimer's disease. Particularly, the subject matter of claims 1 to 11 relates to a vector for inducing Alzheimer's disease in animal model, containing a carboxyl-terminal fragment of human amyloid precursor (hAPP) which contains mutation V717F(βCTF99(V717F)). The subject matter of claims 11 to 13 relates to a transgenic mouse having induced Alzheimer's disease pathology generated by microinjection of the said vector into a pronuclei of a fertilized oocyte followed by generating mice.

D1 discloses a transgenic mouse exhibiting learning and memory performance deficits, and altered emotionality, which overexpresses hAPP carrying the mutation V717F.

D2 discloses a transgene comprising a platelet-derived growth factor promoter, APP carrying the mutation V717F (APPInd), intron, SV40 pA region.

D3 discloses transgenic mice expressing human β-CTF with the I45F mutation under the control of the prion protein promoter.

D4 discloses transgenic mice expressing human β-CTF, which are generated using the transgene of signal peptide and C-terminal 99 residues of APP under the control of CMV enhancer/chicken β-actin promoter.

(Continued on Supplemental Box.)

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of :

Box V. 2

None of the prior art documents D1 to D4 disclose the vector containing only a C-terminal fragment of hAPP carrying V717F mutation (βCTF99V717F), and a transgenic mouse generated by the same.

Thus, the novelty of the subject matter of claims 1 to 13 can be acknowledged [PCT Article 33(2)].

Since there are transgenic mice expressing β-CTF or β-CTF(I45F) to address the potential neurotoxicity of the β-CTF of hAPP (D3, D4), and D1, D2 disclose that V717F mutation of APP alters proteolytic processing of APP and the mouse expressing APP(V717F) exhibits Alzheimer's disease pathology, it appears to be obvious to a person skilled in the art to generate transgenic mice expressing β-CTF carrying V717F mutation from the teachings of D1 to D4.

The claims 1-13 therefore cannot be regarded as meeting the requirement of inventive step [PCT Article 33(3)].

2. Industrial Applicability

The subject matter of claims 1-13 is considered to be industrially applicable [PCT Article 33(4)].